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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/971,344	11/17/97	GOELET	P 04990.0008-2

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1655	55

DATE MAILED: 06/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	08/971,344	GOELET ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94-98,101-104,107-111 and 127-139* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94-98,101-104,107-111 and 127-139* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 17 April 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/971344 is acceptable and a CPA has been established. An action on the CPA follows.

Drawings

2. The drawings remain objected to for reasons of record; see the PTO-948 that was attached to Paper No. 14. Acknowledgement is made of applicant's willingness to file corrected drawings upon notification of allowable subject matter.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 94-98, 101-104, 107-111, and 127-139 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5. The amendment of 17 April 2001 has introduced what is considered to be new matter into claims 94-98, 107-111, and 127-139. More specifically, the originally filed specification and

claims have not been found to provide support for a "polymorphic array." Further, the response of 17 April 2001 does not address where support for this phrase can be found.

The amendment of 17 April 2001 is also considered to introduce new matter by defining the range of allelic frequency to be "at least 0.20" (claim 94, 102, 128, and 138). While claims 102, 128, and 138 are dependent claims, it is noted that an independent claim is to be considered as encompassing every limitation of each of its dependent claims. Accordingly, independent claims 94, 101, 127, and 133, and claims that depend therefrom, are considered to encompass this range and similarly, comprise new matter.

Claims 94-98, 101-104, 107-111, and 127-139 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided and The Presence or Absence of Working Examples

The specification identifies specific areas considered to be the invention and provides a series of examples to support certain embodiments. More specifically, the specification at pages 3-8 set forth in broad terms the following embodiments considered to be the invention:

- "The present invention is directed to molecules that comprise single nucleotide polymorphisms (SNPs) that are resent in mammalian DNA, and in particular, to equine and human genomic DNA polymorphisms." (Page 3, lines 27-30.)
- "The invention particularly concerns the embodiments wherein the mammal is a horse, and when the nucleic acid molecule has a nucleotide sequence selected from the group consisting of SEQ ID NO:(2n+1) [refer to Table 1], wherein n is an integer selected from the group consisting of 0 through 35, or wherein the sequence of the immediately 3'-distal segment includes a sequence selected from the group consisting of SEQ ID NO:(2n+2), wherein n is an integer selected from the group consisting of 0 through 35." (Page 4, lines 17-24.)
- "The invention also provides a method for determining the extent of genetic similarity between DNA of a target horse and DNA of a reference horse" (page 4, lines 33-35).
- "The invention further provides a method for determining the probability that a target horse will have a particular trait" (page 6, lines 12-13).
- "The invention further provides a method for creating a genetic map of a unique sequence equine polymorphisms" (page 6, lines 27-28).

- "The invention further provides a method for predicting whether a target horse will exhibit a predetermined trait," (page 7, lines 17-18).
- "The invention further provides a method for identifying a single nucleotide polymorphic site" (page 8, lines 1-2).
- "The invention also includes a method for interrogating a polymorphic region of a human single nucleotide polymorphism of a target human" (page 8, lines 20-22).

The specification sets forth the following examples:

- Example 1, pages 45-47, "Discovery of Equine Polymorphisms."
- Example 2, pages 47-50, "Characterization of Equine Polymorphisms."
- Example 3, pages 50-54, "Allelic Frequency Analysis of Equine Polymorphisms in Small Population Studies."
- Example 4, page 55, "[Equine] Parentage Testing."
- Example 5, pages 56-58, "[Equine] Identity Testing."
- Example 6, pages 58-62, "Analysis of Human SNP."

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the prior art, based upon what was known in 03 November 1993, the filing date of he priority application, was extremely limited.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

Claims 94-98 and 107-111 have sufficient breadth of scope so to encompass the generation of a genetic map for any and all life forms, without limit to the size of the nucleic acid being used and without restriction on the conditions under which the method is to be practiced.

Claims 101-104, 107-111, and 127-139 have sufficient breadth of scope so to encompass the creation of an association between any SNP variant and "any trait of interest." The "trait of interest" has, for purposes of examination, been considered to encompass not only physiological characteristics, but disease conditions, be they caused by a single gene or by a series of genes through unknown pathways, as well as improved growth and nutritional aspects of any plant or animal. Like the situation with claims 94-98 and 107-111 above, the claimed method has sufficient breadth so to encompass its being practiced under virtually any condition and where the sample is highly heterogeneous.

The claimed method is considered to encompass the use of hybridization reactions. As set forth in Carrico, (US Patent 5,200,313) the extent and specificity of hybridization is affected by the following principal conditions:

1. The purity of the nucleic acid preparation.

2. Base compositions of the probe - G-C base pairs will exhibit greater thermal stability than A-T or A-U base pairs. Thus, hybridizations involving higher G-C content will be stable at higher temperatures.

3. Length of homologous base sequences- Any short sequence of bases (e.g., less than 6 bases), has a high degree of probability of being present in many nucleic acids. Thus, little or no specificity can be attained in hybridizations involving such short sequences. From a practical standpoint, a homologous probe sequence will often be between 300 and 1000 nucleotides.

4. Ionic strength- The rate of reannealing increases as the ionic strength of the incubation solution increases. Thermal stability of hybrids also increases.

5. Incubation temperature- Optimal reannealing occurs at a temperature about 25 - 30 °C below the melting temperature for a given duplex. Incubation at temperatures significantly below the optimum allows less related base sequences to hybridize.

6. Nucleic acid concentration and incubation time- Normally, to drive the reaction towards hybridization, one of the hybridizable sample nucleic acid or probe nucleic acid will be present in excess, usually 100 fold excess or greater.

7. Denaturing reagents- The presence of hydrogen bond-disrupting agents, such as formaldehyde and urea, increases the stringency of hybridization.

8. Incubation- The longer the incubation time, the more complete will be the hybridization.

9. Volume exclusion agents- The presence of these agents, as exemplified by dextran and dextran sulfate, are thought to increase the effective concentrations of the hybridizing elements thereby increasing the rate of resulting hybridizations.

Further, subjecting the resultant hybridization product to repeated washes or rinses in heated solutions will remove non-hybridized probe. The use of solutions of decreasing ionic strength, and increasing temperature, e.g., 0.1X SSC for 30 minutes at 65 °C, will, with increasing effectiveness, remove non-fully complementary hybridization products.

The specification does not set forth in sufficient detail just how these art-recognized problems are to be overcome sans the skilled artisan having to resort to undue experimentation. As applicant has carefully and repeatedly indicated at the beginning of the specification, the invention contemplated by applicant at the time of filing, was directed to the use of specific markers in determining the parentage of thoroughbred horses. The claims now before the office are only tangentially related to such an invention. Clearly, the specification does not disclose in sufficient detail how any trait in any life form can be associated with one or more SNPs. Further, to practice such an invention, one would have to first know what the SNPs are for any species. In addition, given the scope of the claims, one would have to know the SNPs for every life form in the world to be capable of practicing the claimed invention to the fullest extent of the claims. Even at this late date, the art has not progressed to the point that one would be able to provide a comparison of all SNPs, be they of any breed of horse or for a human, much less for all other life forms. By not setting forth the reaction conditions and the starting materials that would be

needed t practice the claimed invention to its fullest extent, applicant has shifted the burden of enablement from self to that of the public. Such shifting is both improper and creates an unfair burden upon the public. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
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> *****
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> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

For the above reasons, and in the absence of convincing evidence t the contrary, the claims are not considered to be enabled by the specification and as such, are rejected under 35 USC 112, first paragraph.

Conclusion

6. This is a CPA of applicant's earlier Application No. 08/971,344. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephanie Zitomer can be reached on (703) 308-3985. The fax telephone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1655

bls
May 31, 2001